

therefrom. No new limitations were added to either Claim 1 or Claim 10 in this regard, so that no new matter has been introduced by amending these claims to remove statements of intended use and process limitations.

Finally, Claims 2, 3, 5, 9, 14, 17-21, 23, 24, 26 and 27 have been amended to conform with the changes to Claims 1 and 10. Therefore, the amendments to these claims also do not introduce new matter.

For reasons which are submitted below, the claims are believed to be in condition for allowance. The amendments to the specification and claims are believed to resolve the concerns raised by the Examiner. Accordingly, reconsideration is respectfully requested.

In the Official Action, the Examiner at paragraphs 8-10 objected to the disclosure because the chemical structures of Formula I and Formula II were incomplete. The specification has been amended to correct these deficiencies using information contained in the original claims. By amending the specification in this manner, this objection by the Examiner has thus been overcome. Acknowledgment of this by the Examiner and withdrawal of her objections is respectfully requested.

Next, the Examiner at paragraphs 11-13 requested that the claims be amended to remove intended use language. As noted above, Claims 1 and 10 have been amended as requested by the Examiner. Acknowledgment by the Examiner that her objections contained in paragraphs 11-13 have been resolved is respectfully requested.

Next, Claims 1-3, 5, 9, 10, 14, 17-21, 23, 24, 26 and 27 were rejected under 35 U.S.C. § 112, first paragraph for non-enablement. The Examiner stated:

... the specification, while being enabling for a copolymer array of polyacrylate copolymers and methods for the synthesis of said polyacrylate copolymers prepared by the condensation of ... tyrosine-derived diphenol compounds and ... dicarboxylic acids ... **does not reasonably provide** enablement for **all** copolymer arrays comprising a plurality of **all** co-polymers polymerized from two independent variable set of ... monomer ... [(emphasis by Examiner)].

This rejection is respectfully traversed in view of the above claim amendments for the reasons set forth hereinafter.

The present invention is directed to polymer libraries prepared by the parallel synthesis of different copolymers from at least two independently and homologically variable sets of monomers. In the example referred to by the Examiner as polyacrylates (it is believed that the Examiner meant polyarylates, which are the condensation product of the diphenols and dicarboxylic acids that the Examiner refers to), a library of A-B type copolymers is

formed by separately reacting in parallel all possible combinations of Monomer A (a group of homologically varying diphenols) and Monomer B (a group of homologically varying dicarboxylic acids).

As explained in the present specification, the polymer libraries of the present invention can be constructed from essentially any combination of A-type and B-type monomers known to react together to form copolymers. This is reflected in the presently pending claims, which require that the first and second monomer series contain polymerizable functional groups that react together to form copolymers. Libraries of terpolymers and higher can be constructed by introducing third and higher monomers series having polymerizable functional groups that are reactive with the polymerizable functional groups of the first and second monomer series.

In addition to the diphenols and dicarboxylic acid depicted in the examples, the specification also discloses that the hydroxyl group-containing first monomer series need not be diphenols, but also include di-hydroxyl compounds in general (see page 9, lines 12-13). One of ordinary skill in the art readily understands how to prepare a polyester from diol and dicarboxylic acid.

The specification also discloses that amino groups may be substituted for the hydroxyl groups of the first monomer series. Undergraduate chemistry courses teach that polyamides such as NYLON are formed by reacting such diamines with dicarboxylic acids. The specification also discloses that diphenol, dihydroxy and diamine first monomer compounds can also be reactive with di-isocyanates, diesters and anhydrides. A-B-C type polymer libraries may be constructed by introducing the set of homologically varying alkylene oxide monomers, for example that are either are block or random polymerized with monomers from the first and second monomers series.

Thus, the claimed polymer libraries may be constructed from homologous series of monomer types known to react to form copolymers. This was acknowledged by the Examiner when rejecting all of the claims under consideration as being prima facie obvious in view of the polyiminocarbonates of Kohn et al., U.S. Patent No. 4,980,449 when viewed in combination with the Gordon et al. journal article and Still et al., U.S. Patent No. 5,565,324. The Examiner disingenuously overlooks this contention when rejecting the claims for asserted non-enablement.

The claims are limited to polymer libraries prepared from combinations of monomers that are capable of reacting to form polymers. The prior art literature is replete with such monomer combinations. The present invention resides in the parallel and separate synthesis of polymers from combinations of homologically varying series of such monomers. The specification thus clearly enables one of ordinary skill in the art to practice the invention as

defined by the claims, so that the claims therefore satisfy the enablement requirements of 35 U.S.C. § 112, first paragraph, in all respects. Reconsideration by the Examiner and withdrawal of this rejection is therefore respectfully requested.

Next, in paragraph 16 of the Official Action, Claims 1-3, 5, 9, 10, 14, 17-21, 23, 24, 26 and 27 were rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. No reason was given for this rejection, which is respectfully traversed for this reason. The Examiner is requested to identify the basis for her indefiniteness rejection in paragraph 16 of the Official Action.

Next, Claims 1, 3, 10 and 19 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention. The Examiner's objection to these claims will be addressed in the order presented by the Examiner.

In Claim 1, the Examiner considered the terms "multi-dimensional copolymer array," "variable sets of monomers," "non-varying polymerizable functional groups," "two different structural features of said copolymer" and "one end-use property of said polymer" to be indefinite. These rejections are respectfully traversed in view of the above amendment to Claim 1 for the reasons set forth herein after.

In Claim 1, the term "multi-dimensional copolymer array" has been replaced with "copolymer library," to clarify that the claim is directed to a set of copolymers constructed from homologically varying series of monomers. The term "variable sets of monomers" in the claim preamble has been deleted. The term "non-varying polymerizable functional groups" has been replaced with "the same polymerizable functional groups." In other words, all the monomers within a monomer series have the same polymerizable functional groups. This also means that a homologous variation within each monomer series does not occur at the site of polymerization. This ensures that the homologous variation within each monomer series is passed along to each polymer of the polymer library. As explained at page 5 of the present specification, the homologous variations within each monomer series are selected to minimize any effect upon the reactivity of the polymerizing functional groups of the monomers within each series.

Homologous series are specifically defined not only as relating to substituent groups on a series of monomers, but also including variations within the monomer backbone structure such as the introduction of unsaturation, the inclusion of additional methylene units, the replacement of a methylene carbon with a nitrogen or any other suitable atom, the replacement of a methylene unit with an oxygen or sulfur atom, or any other suitable atom, the replacement of a methylene unit with another unit including, but not limited to, a keto-

unit, an amide unit, or an ester unit. In other words, not only does the present specification provide examples of polymerizable functional groups, the specification also identifies where, other than at the polymerizable functional groups, the homologous variation of each monomer series occurs.

The meaning of the term "the same polymerizable functional groups" is therefore unambiguous. Acknowledgment of this by the Examiner and withdrawal of this aspect of the rejection of Claim 1 under 35 U.S.C. § 112, second paragraph is therefore respectfully requested.

Otherwise, the "two different structural features of said copolymer" and "one end-use property of said copolymer" terms objected to by the Examiner have also been deleted. Other than the term demonstrated above to be unambiguous, the language of Claim 1 objected to by the Examiner has been removed. Accordingly, the Examiner's rejection of Claim 1 under 35 U.S.C. § 112, second paragraph has thus been overcome. Reconsideration and withdrawal by the Examiner of the Claim 1 rejections is therefore respectfully requested.

Claim 3 was rejected under 35 U.S.C. § 112, second paragraph because the Examiner considered the claim term "wherein said free-radical process is [an] ionic polymerization" to be vague and indefinite. The Examiner pointed out that ionic and free-radical polymerizations involve different mechanisms. This rejection is respectfully traversed in view of the above amendment to Claim 3 for the reasons set forth hereinafter.

Claim 3 has been amended to differentiate ionic polymerization from free-radical polymerization. This removes the ambiguity from Claim 3. By amending Claim 3 in this manner, this rejection by the Examiner of Claim 3 for indefiniteness under 35 U.S.C. § 112, second paragraph is thus overcome. Reconsideration by the Examiner and withdrawal of this rejection is therefore respectfully requested.

Claim 10 was rejected by the Examiner under 35 U.S.C. § 112, second paragraph for containing the same language objected to by the Examiner with respect to Claim 1. In addition, the Examiner also objected to the term "condensation-type." This rejection is respectfully traversed in view of the above amendments to Claim 10 for the reasons set forth hereinafter.

The language objected to by the Examiner that was deleted from Claim 1 has also been deleted from Claim 10. As in Claim 1, the term "non-varying polymerizable functional groups" has been replaced with "the same polymerizable functional groups," which is non-ambiguous for the reasons given above with respect to Claim 1. Finally, the term "condensation-type copolymer array" has been replaced with "condensation polymer library." What constitutes a condensation polymer is well-understood by those of ordinary skill in the art.

Claim 10 as amended is therefore is also unambiguous. By amending Claim 10 in this manner, the Examiner's rejection of this claim as being indefinite under 35 U.S.C. § 112, second paragraph has thus been overcome. Reconsideration by the Examiner and withdrawal of this rejection is therefore respectfully requested.

Claim 19 was rejected by the Examiner under 35 U.S.C. § 112, second paragraph because the term "random and block polymers and copolymers thereof" was consider vague and indefinite. The Examiner also questioned with the term "ionic polymerization" refers to. This rejection is respectfully traversed in view of the above amendment to Claim 19 for the reasons set forth hereinafter.

To begin with, the term "ionic polymerization" does not appear in Claim 19. Clarification by the Examiner of this portion of the rejection is respectfully requested.

As for the term "random and block polymers and copolymer thereof," the specification states at page 9, line 24-27 that an alkylene oxide monomer series can include "ethylene oxide, propylene oxide, isopropylene oxide, butylene oxide, isobutylene oxide and block and random copolymer segments thereof. It is well known that alkylene oxides may be introduced into polymers by randomly introducing individual alkylene oxide units, or by copolymerizing "blocks" of alkylene oxides. Each block can be a block of a single alkylene oxide, or it can consist of sub-blocks of two or more different alkylene oxides, or can consist of a block of several randomly polymerized alkylene oxides. In view of the foregoing, which is understood by those having ordinary skill in the art, the meaning of the term "random and block polymers and copolymers thereof" as it relates to the listed alkylene oxides of Claim 19 is unambiguous. In view of the foregoing explanation, reconsideration by the Examiner and withdrawal of the rejection of Claim 19 as being indefinite under 35 U.S.C. § 112, second paragraph is therefore respectfully requested.

Next, Claims 1-3, 5, 9, 10, 14, 17-21, 23, 24, 26 and 27 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kohn et al. U.S. Patent No. 5,216,115, when viewed in combination with the Gordon et al. journal article and Still et al., U.S. Patent No. 5,565,324. Kohn et al. was cited as disclosing the synthesis of the claimed polyarylates and their intended uses. The Examiner acknowledges that the Kohn patent does not disclose the synthesis of multi-dimensional polyarylate arrays, but cites the Gordon et al. journal article and the Still et al. patent as teaching this. Specifically, Gordon et al. is cited as teaching "when small molecule leads for a target have been previously defined, the notion of searching for more potent derivatives among libraries combinatorially enriched in specific pharmacophore analogs is an obvious tactic to pursue." The Examiner also refers to Gordon et al.'s use of a "spectrum of molecular diversity" strategy in the generation of a library or array composed of a few to many molecules. The Examiner also quotes Gordon et al. as

stating that "a key aspect in the successful application of combinatorial technologies to drug discovery is the requirement for having a closely linked coordinated process for the integration of synthesis and screening." Still et al. is cited as teaching the basic tools for combinatorial organic synthesis. This rejection is respect-fully traversed in view of the above claim amendments for the reasons set forth hereinafter.

Gordon et al. discloses the single pot synthesis of small molecules employing building blocks of approximately 150 dalton molecular weight. Gordon et al. represents the classic approach to the combinatorial synthesis of small compounds in a single vessel to create libraries to be analyzed by simple biological screening procedures to fish out lead compounds from the many species present in such single pot libraries.

The presently claimed invention, on the other hand, is directed to the separate and parallel synthesis of individual polymers that are prepared as clean, neat sample materials. Homogeneity with respect to structure and molecular weight are critical.

Furthermore, Still et al. excludes polymers. Instead, the teaching of Still et al. is directed to "oligomers and synthetic non-repetitive organic molecules."

The one pot synthesis of Gordon et al. and the non-polymers of Still et al. thus teach against the presently claimed invention. The cited prior art thus fails to teach or suggest the presently claimed polymer libraries constructed from separately synthesized polymers.

By amending Claims 1 and 10 to emphasize this distinction, this rejection of Claims 1-3, 5, 9, 10, 14, 17-21, 23, 24, 26 and 27 under 35 U.S.C. § 103(a) in view of the cited combination of prior art has thus been overcome. Reconsideration by the Examiner and withdrawal of this rejection is therefore respectfully requested.

Claims 1-3, 5, 9, 10, 14, 17-21, 23, 24, 26 and 27 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kohn et al., U.S. Patent No. 4,980,449, when viewed in combination with the above-cited Gordon et al. journal article and Still et al. patent. Essentially the same re-jection was made, with the Kohn et al. '449 patent cited as teaching polymers and polymerization processes of the invention not disclosed by the Kohn et al. '115 patent. This rejection is respect-fully traversed in view of the above claim amendments for the reasons set forth hereinafter.

Regardless of what is disclosed by the Kohn et al. '449 patent, the claims under rejection nevertheless remain patentably distinguishable over the cited combination of prior art because of the manner in which the Gordon et al. journal article and Still et al. patent teach against the invention as presently claimed. That is, the separate and parallel synthesis techniques employed to construct the presently claimed polymer libraries that are neither taught nor suggested by Gordon et al. or Still et al. are not supplied by the teachings of the

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Kohn et al. '449 patent. In other words, Claims 1-3, 5, 9, 10, 14, 17-21, 24 and 27 patentably distinguish over the cited combination of Kohn et al. '449, Gordon et al. and Still et al. under 35 U.S.C. § 103(a) for the reasons given above with respect to Kohn et al. '115, Gordon et al. and Still et al.

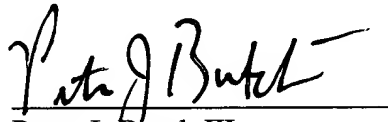
By amending Claims 1 and 10 to emphasis that the library polymers are separately polymerized this rejection of Claims 1-3, 5, 9, 10, 14, 17-21, 24 and 27 under 35 U.S.C. § 103(a) as being unpatentable over the cited combination of Kohn et al. '449, Gordon et al. and Still et al. has thus been overcome. Reconsideration by the Examiner and withdrawal of this rejection is therefore respectfully requested.

Accordingly, in view of the above amendments to the specification and claims, and the foregoing remarks, this application is now in condition for allowance. Reconsideration is respectfully requested. Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE.**"

If the Examiner still believes that there are any objections to this application, she is requested to telephone the undersigned. If there are additional charges in connection with this amendment, the Examiner is authorized to charge Applicant's Deposit Account No. 19-5425 therefor.

Respectfully submitted,

Dated: August 3, 2001


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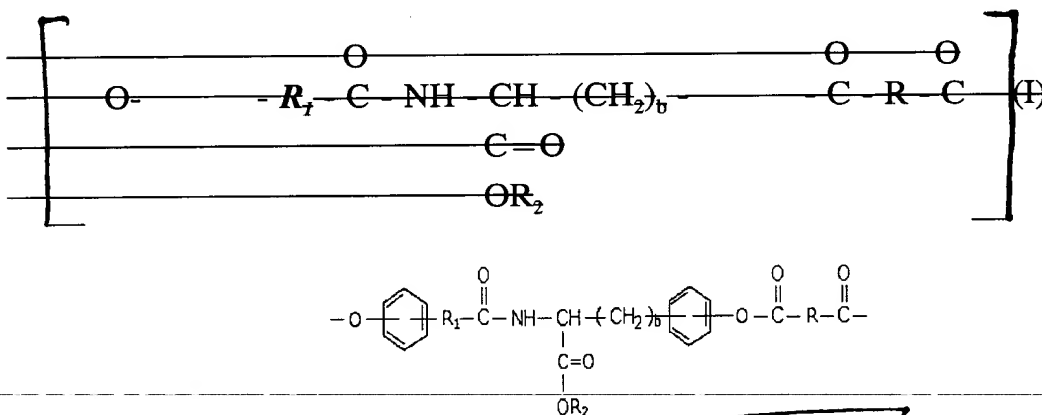
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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification

The paragraph at page 6, lines 14-27 has been amended to read as follows:

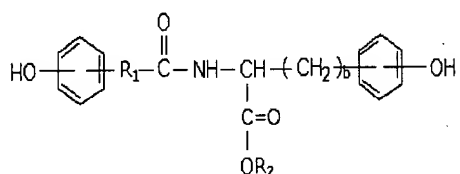
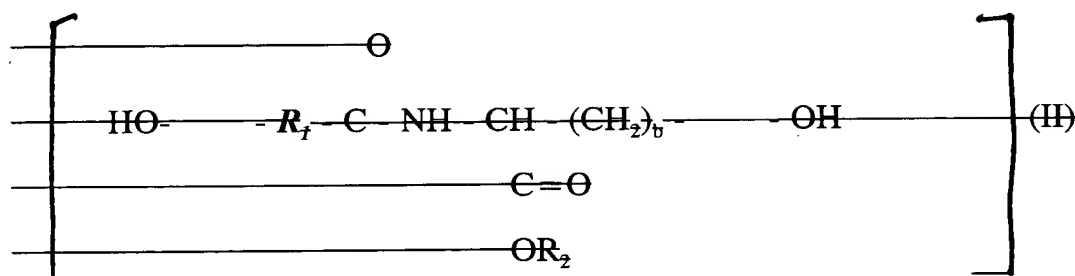
Through the use of the inventive methodology it was unexpectedly discovered that polyarylate copolymers, prepared by the condensation of a tyrosine-derived diphenol compound and a dicarboxylic acid, and having an ether linkage in either the polymer backbone or the polymer side chain were good cell growth substrates despite being very hydrophobic. Therefore, according to another aspect of the present invention, polyarylates are provided having repeating units with the structure of Formula I:



wherein R is selected from saturated and unsaturated, substituted and unsubstituted, alkyl and alkylaryl groups containing up to 18 carbon atoms;

The paragraph at page 7, lines 8-24 has been amended to read as follows:

The polyarylate copolymers of the present invention having ether linkage-containing side chains are the condensation product of a dicarboxylic acid with a tyrosine-derived diphenol compound having at least one side chain containing at least one ether linkage. These diphenol compounds are novel and non-obvious in view of their unexpected ability to condense with a dicarboxylic acid to form a polyarylate copolymer that is unexpectedly both a good cell growth substrate and very hydrophobic. Therefore, according to another aspect of the present invention, a tyrosine-derived diphenol compound is provided having the structure of Formula II:



wherein R_1 , R_2 , and b are the same as described above with respect to Formula I, with the proviso that R_2 , and/or, when R_1 is $-\text{CHNL}_1\text{L}_2$, at least one of L_1 and L_2 , contains at least one ether linkage.

In the Claims

Claims 1-3, 5, 9, 10, 14, 17-21, 23, 24, 26 and 27 have been amended as follows:

1. (Amended) A ~~multidimensional~~ copolymer library array, comprising a plurality of different copolymers, each separately polymerized from (1) a first monomer selected from the group consisting of at least two independently variable sets of monomers, wherein said polymerization is characterized by:

~~— (a) — selecting~~ a first homologously varying series of monomers with the same non-varying polymerizable functional groups; and (2) a second monomer selected from the group consisting of a

~~(b) — selecting at least one additional~~ homologously varying series of second different monomers having the same non-varying polymerizable functional groups that are reactive with the polymerizable functional groups of said first series of monomers to form copolymers; and

~~— (c) — separately reacting a plurality of monomers from said first monomer series with a plurality of monomers from each of said additional monomer series to form said plurality of copolymers;~~

~~wherein said homologous variations of said monomer series are selected to determine the effect of independently varying at least two different structural features of said copolymer on at least one end-use property of said copolymer.~~

2. (Amended) The copolymer library array of Claim 1, wherein said copolymers are formed by polymerization reaction is a free-radical polymerization process.

3. (Amended) The copolymer library array of Claim ~~2~~ 1, wherein said copolymers are formed by free-radical process is an ionic polymerization.

5. (Amended) The copolymer library array of Claim 1, wherein said ~~separate reactions are performed~~ copolymers are separately polymerized in solution.

9. (Amended) The copolymer library array of Claim 1, wherein said copolymers are further modified by chemical reactions or cross-linking.

10 (Amended) A ~~multi-dimensional condensation-type copolymer polymer library array,~~ comprising a plurality of different copolymers, each separately polymerized from at least two independently variable sets of monomers, wherein said polymerization is characterized by:

~~—(a) selecting~~ (1) a first monomer selected from the group consisting of a first homologically varying series of monomers with the same ~~non-varying~~ polymerizable functional groups; and

~~—(b) selecting at least one additional~~ (2) a second monomer selected from the group consisting of a homologically varying series of second-different monomers having ~~non-varying the same~~ polymerizable functional groups that are reactive with the polymerizable functional groups of said first series of monomers to condense to form copolymers; and

~~—(c) separately reacting a plurality of monomers from said first monomer series with a plurality of monomers from each of said additional monomer series to form said plurality of condensation-type copolymers;~~

~~—wherein said homologous variations of said monomer series are selected to determine the effect of independently varying at least two different structural features of said copolymer on at least one end-use property of said copolymer.~~

14. (Amended) The polymer library ~~copolymer array~~ of Claim 10, wherein said ~~separate reactions are performed~~ copolymers are separately polymerized in solution.

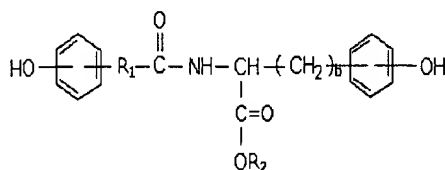
17. (Amended) The polymer library ~~copolymer array~~ of Claim 10, wherein said ~~separate reactions are performed~~ copolymers are separately polymerized in the absence of a catalyst.

18. (Amended) The polymer library ~~copolymer array~~ of Claim 10, wherein said polymerizable functional groups of said first monomer series are amine or hydroxyl groups and said polymerizable functional groups of said ~~additional~~ second series of monomers are selected from the group consisting of carboxylic acids, esters, anhydrides and isocyanates.

19. (Amended) The polymer library ~~copolymer array~~ of Claim 18, wherein said ~~additional series of monomers comprise second and third monomer series, said second monomer series is selected from the group consisting of carboxylic acids, esters, anhydrides and isocyanates, and said third monomer series comprises a plurality of alkylene oxides~~ plurality of different copolymers comprises a plurality of different terpolymers each separately polymerized from said first and second groups of monomers and a third monomer selected from the group consisting of ethylene oxide, propylene oxide, isopropylene oxide, butylene oxide, isobutylene oxide and random and block polymers and copolymers thereof.

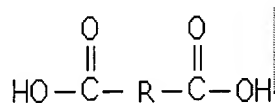
20. (Amended) The polymer library ~~copolymer array~~ of Claim 18, wherein said polymerizable functional groups of said first monomer series are hydroxyl groups and said ~~additional monomer series comprise a~~ polymerizable functional groups of said second monomer series ~~with polymerizable~~ are carboxylic acid groups.

21. (Amended) The polymer library ~~copolymer array~~ of Claim 20, wherein said first monomer series comprises a plurality of different diphenol compounds, each having the general structure:



wherein R_1 is selected from the group consisting of $-\text{CH}=\text{CH}-$, $(\text{CH}_2)_a$, and $-\text{CHN}(\text{L}_1\text{L}_2)$, in which a has a value from zero to eight, inclusive, and L_1 and L_2 are independently selected from the group consisting of hydrogen and straight and branched alkyl and alkylaryl groups containing up to 18 carbon atoms, provided that L_1 and L_2 are not both hydrogen; b independently has a value between 0 and 8, inclusive; and R_2 is selected from the group consisting of straight and branched alkyl and alkylaryl groups containing up to 18 carbon atoms.

23. (Amended) The polymer library ~~copolymer array~~ of Claim 20, wherein said second monomer series ~~with polymerizable carboxylic acid groups~~ comprises a plurality of different dicarboxylic acid compounds, each having the general structure:



wherein R is selected from the group consisting of saturated and unsaturated, substituted and unsubstituted alky, aryl and alkylaryl groups containing up to 18 carbon atoms.

24. (Amended) The polymer library ~~copolymer array~~ of Claim 21, wherein for one or more of said monomers of said first monomer series, at least one of R_2 , L_1 or L_2 contain at least one ether linkage.

26. (Amended) The polymer library ~~copolymer array~~ of Claim 23, wherein for one or more of said monomers of said dicarboxylic acid monomer series, R contains at least one ether linkage.

27. (Amended) The polymer library ~~copolymer array~~ of Claim 10, wherein said copolymers are further modified by chemical reactions or cross-linking.